

Claims

What is claimed is:

1. A method for producing a bone-polymer composite comprising: (a) providing a plurality of bone particles; (b) treating the bone particles with a coupling agent; and (c) incorporating the bone particles obtained from (b) into a polymer.

2. The method of claim 1, wherein the bone particles are obtained from one or more of autologous bone, allogenic bone, xenogenic bone, and mixtures thereof.

3. The method of claim 1, wherein the bone particles are obtained from one or more of cortical bone, cancellous bone, cortico-cancellous bone, and mixtures thereof.

4. The method of claim 1, wherein the bone particles are obtained from one or more of nondemineralized bone, deorganified bone, anorganic bone, and mixtures thereof.

5. The method of claim 1, wherein the coupling agent is selected from silanes, zirconates, and titanates.

6. The method of claim 1, wherein the coupling agent is a silane selected from silanes bearing one hydrolyzable or leaving group, silanes bearing two hydrolyzable or leaving groups, and silanes bearing three hydrolyzable or leaving groups.

7. The method of claim 1, wherein the polymer is a biocompatible polymer selected from polymers of natural origin, polymers of artificial origin, and any combination of natural and artificial polymers.

8. The method of claim 1, wherein the polymer is a selected from biodegradable polymers, non-biodegradable polymers, co-polymers of biodegradable polymers, co-polymers of non-biodegradable polymers, and co-polymers of biodegradable and non-biodegradable polymers.

9. The method of claim 1, wherein the polymer is a natural polymer selected from polysaccharides and proteins.

10. The method of claim 9, wherein the polymer is selected from starch, dextran, cellulose, derivatives of the above, gelatin, and collagen.

11. The method of claim 1, wherein the polymer is an artificial polymer selected from poly(anhydrides), poly(hydroxy acids), polyesters, poly(orthoesters), polycarbonates, poly(propylene fumarates), poly(caprolactones), polyamides, polyamino acids, polyacetals, polylactides, polyglycolides, polysulfones, poly(dioxanones), polyhydroxybutyrates, polyhydroxyvalyrates, poly(vinyl pyrrolidones), biodegradable polycyanoacrylates, biodegradable polyurethanes, polysaccharides, tyrosine-based polymers, poly(methyl vinyl ether), poly(maleic anhydride), poly(glyconates), polyphosphazines, poly(esteramides), polyketals, poly(orthocarbonates), poly(maleic acid), poly(alkylene oxalates), poly(alkylene succinates), poly(pyrrole), poly(aniline), poly(thiophene), polystyrene, non-biodegradable polyurethanes, polyureas, poly(ethylene vinyl acetate), polypropylene, polymethacrylate, polyethylene, poly(ethylene oxide), and co-polymers, adducts, and mixtures thereof.

12. The method of claim 6, wherein the silane coupling agent attached to the bone particles is linked to the polymer by a member of covalent and non-covalent interactions.

13. The method of claim 6, further comprising chemically modifying the silane coupling agent.

14. The method of claim 13, wherein chemically modifying comprises attaching a moiety selected from a biomolecule, a small molecule, a bioactive agent, a non-biologically active material, and any combination of the above to the silane coupling agent.

15. The method of claim 14, wherein the moiety is linked to the polymer by a member of covalent and non-covalent interactions.

16. The method of claim 1, further comprising the step of modifying a surface of at least a portion of the bone particles before treatment with the coupling agent.

17. The method of claim 16, wherein modifying comprises treating the bone particles with dilute phosphoric acid.

18. The method of claim 1, further comprising the step of modifying a composition of the bone particles before treatment with the coupling agent.

19. The method of claim 18, wherein modifying comprises one or more of drying the bone particles, lyophilizing the bone particles, defatting the bone particles, treating the bone particles with a detergent, treating the bone particles with a solvent, treating the bone particles with a surfactant, removing pathogens, and inactivating pathogens.

20. The method of claim 19, wherein removing pathogens comprises one or more of radiation sterilization, antibiotic treatment, and treatment with a pathogen-inactivating chemical.

21. The method of claim 19, wherein inactivating pathogens comprises one or more of radiation sterilization, antibiotic treatment, and treatment with a pathogen inactivating chemical.

22. The method of claim 1, wherein step (c) further includes combining a cross-linking agent with treated bone particles and the polymer.

23. The method of claim 22, wherein the cross-linking agent is selected from the group consisting of aldehydes, polyepoxy compounds, polyvalent metallic oxides, organic tannins, N-hydroxysuccinimides, N-hydroxysulfosuccinimides, phenolic oxides, hydrazides, carbodiimides, isocyanates, isothiocyanates, sugars and enzymes.

24. The method of claim 1, wherein step (c) comprises solvent casting, melting, or both.

25. The method of claim 1, further comprising modifying a surface of the composite.

26. The method of claim 25, wherein the step of modifying a surface of the composite comprises one or more of oxidizing at least a portion of the surface, etching at least a portion of the surface, retaining a biomolecule on the surface, retaining a small molecule on the surface, retaining a bioactive agent on the surface, and any combination of the above.

27. The method of claim 1, further comprising combining the composite with one or more of a wetting agent, biocompatible binder, filler, fiber, plasticizer, biostatic/biocidal agent, surface active agent, biomolecule, small molecule, and bioactive agent.

28. The method of claim 27, wherein the biologically active agent is selected from antibiotics, chemotherapeutics, bone cell inducers, and bone cell stimulators.

29. The method of claim 1, further comprising incorporating osteoblasts into the composite.

30. The method of claim 1, 25 or 27, further comprising processing the composite to obtain an osteoimplant having a desired shape.

31. The method of claim 30, wherein the processing comprises a fabrication technique selected from injection molding, casting, machining, vacuum forming, blow molding, extruding, and any combination of the above fabrication techniques to obtain the desired form of a solid graft.

32. The method of claim 30, wherein the shape of the osteoimplant is selected from the group consisting of a bone, a section of a bone, sheet, plate, particle, sphere, strand, coiled strand, capillary network, film, fiber, mesh, disk, cone, pin, screw, tube, cup, tooth, tooth root, strut, wedge, portion of wedge, cylinder, threaded cylinder, and rod.

33. The method of claim 30, further comprising coating an outer portion of the implant with a biodegradable polymer that is substantially non-porous and substantially impermeable to bodily fluids.

5 34. A composite, comprising:
a plurality of bone particles and a biocompatible polymer, wherein at least a portion of the bone particles are covalently linked to the polymer through a silane coupling agent.

10 35. The composite of claim 34, wherein the bone particles are obtained from one or more of autologous bone, allogenic bone, xenogenic bone, and mixtures thereof.

36. The composite of claim 34, wherein the bone particles are obtained from one or more of cortical bone, cancellous bone, cortico-cancellous bone and mixtures thereof.

15 37. The composite of claim 34, wherein the bone particles are obtained from one or more of nondemineralized bone, deorganified bone, anorganic bone, and mixtures thereof.

38. The composite of claim 34, wherein the bone particles represent about 60% to about 75% of the total weight of the composite.

20 39. The composite of claim 34, wherein the coupling agent is a silane selected from silanes bearing one hydrolyzable or leaving group, silanes bearing two hydrolyzable or leaving groups, and silanes bearing three hydrolyzable or leaving groups.

25 40. The composite of claim 34, wherein the polymer is a biocompatible polymer selected from polymers of natural origin, polymers of artificial origin and any combination of natural and artificial polymers.

30 41. The composite of claim 34, wherein the polymer is a selected from biodegradable polymers, non-biodegradable polymers, co-polymers of biodegradable polymers, co-polymers of

non-biodegradable polymers, and co-polymers of biodegradable and non-biodegradable polymers.

42. The composite of claim 34, wherein the polymer is a natural polymer selected from polysaccharides.

43. The composite of claim 42, when the polymer is selected from starch, dextran, cellulose, derivatives thereof, gelatin, and collagen.

44. The composite of claim 34, wherein the polymer is an artificial polymer selected from poly(anhydrides), poly(hydroxy acids), polyesters, poly(orthoesters), polycarbonates, poly(propylene fumarates), poly(caprolactones), polyamides, polyamino acids, polyacetals, polylactides, polyglycolides, poly(dioxanones), polysulfones, polyhydroxybutyrates, polyhydroxyvalyrates, poly(vinyl pyrrolidone), biodegradable polycyanoacrylates, biodegradable polyurethanes, polysaccharides, tyrosine-based polymers, poly(methyl vinyl ether), poly(maleic anhydride), poly(glyconates), polyphosphazines, poly(esteramides), polyketals, poly(orthocarbonates), poly(maleic acid), poly(alkylene oxalates), poly(alkylene succinates), poly(pyrrole), poly(aniline), poly(thiophene), polystyrene, non-biodegradable polyurethanes, polyureas, poly(ethylene vinyl acetate), polypropylene, polymethacrylate, polyethylene, poly(ethylene oxide), and co-polymers, adducts, and mixtures thereof.

45. The composite of claim 34, wherein at least a portion of the silane coupling agent attached to the bone particles is chemically modified.

46. The composite of claim 45, wherein a moiety selected from a biomolecule, a small molecule, a bioactive agent, a non-biologically active material, and any combination of the above is attached to the silane coupling agent.

47. The composite of claim 45, wherein the moiety is linked to the polymer by a member of covalent and non-covalent interactions.

48. The composite of claim 34, wherein a surface of at least a portion of the bone particles has been chemically modified.

49. The composite of claim 48, wherein the surface of at least a portion of the bone particles is treated with dilute phosphoric acid.

50. The composite of claim 34, wherein the composition of the bone particle has been modified.

51. The method of claim 50, wherein at least a portion of the bone particles are dried, lyophilized, defatted, treatment with a detergent, treatment with a solvent, treatment with a surfactant, or treated to remove or inactivate pathogens.

52. The composite of claim 34, further comprising a cross-linking agent.

53. The composite of claim 52, wherein the cross-linking agent is selected from aldehydes, polyepoxy compounds, polyvalent metallic oxides, organic tannins, N-hydroxysuccinimides, N-hydroxysulfosuccinimides, phenolic oxides, hydrazides, carbodiimides, isocyanates, isothiocyanates, sugars and enzymes.

54. The composite of claim 34, wherein a surface of the composite is modified.

55. The composite of claim 54, wherein the modification of a surface of the composite is a member of oxidation of at least a portion of the surface, etching of at least a portion of the surface, retention of a biomolecule on the surface, retention of a small molecule on the surface, retention of a bioactive agent on the surface, and any combination of the above.

56. The composite of claim 34, further comprising one or more of a wetting agent, biocompatible binder, filler, fiber, plasticizer, biostatic/biocidal agent, surface active agent, biomolecule, small molecule, bioactive agent.

57. The composite of claim 56, wherein the biologically active agent is selected from antibiotics, chemotherapeutics, bone cell inducers, and bone cell stimulators.

58. The composite of claim 34, further comprising osteoblasts.

59. A load-bearing osteoimplant, comprising: a composite comprising a biocompatible polymer and bone particles, wherein at least a portion of the bone particles are covalently linked to the polymer through a silane coupling agent, and the biocompatible polymer is not a polyaromatic polymer.

60. The osteoimplant of claim 59, wherein the bone particles are obtained from one or more of autologous bone, allogenic bone, xenogenic bone, and mixtures thereof.

61. The osteoimplant of claim 59, wherein the bone particles are obtained from one or more of cortical bone, cancellous bone, cortico-cancellous bone and mixtures thereof.

62. The osteoimplant of claim 59, wherein the bone particles are obtained from one or more of nondemineralized bone, deorganified bone, anorganic bone, and mixtures thereof.

63. The osteoimplant of claim 59, wherein the bone particles represent about 60% to about 75% of the total weight of the composite.

64. The osteoimplant of claim 59, wherein the coupling agent is a silane selected from silanes bearing one hydrolyzable or leaving group, silanes bearing two hydrolyzable or leaving groups, and silanes bearing three hydrolyzable or leaving groups.

65. The osteoimplant of claim 59, wherein the biocompatible polymer is selected from polymers of natural origin, polymers of artificial origin and any combination of natural and artificial polymers.

66. The osteoimplant of claim 59, wherein the polymer is selected from biodegradable polymers, non-biodegradable polymers, co-polymers of biodegradable polymers, co-polymers of non-biodegradable polymers, and co-polymers of biodegradable and non-biodegradable polymers.

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67. The osteoimplant of claim 59, wherein the polymer is a natural polymer selected from polysaccharides and proteins.

68. The osteoimplant of claim 67, wherein the polymer is selected from starch, dextran,
10 cellulose, derivatives of the above, gelatin, and collagen.

69. The osteoimplant of claim 59, wherein the polymer is an artificial polymer selected from poly(anhydrides), poly(hydroxy acids), polyesters, poly(orthoesters), polycarbonates, poly(propylene fumarates), poly(caprolactones), polyamides, polyamino acids, polyacetals,
15 polylactides, polyglycolides, poly(dioxanones), polysulfones, polyhydroxybutyrates, polyhydroxyvalyrates, poly(vinyl pyrrolidone), biodegradable polycyanoacrylates, biodegradable polyurethanes, polysaccharides, tyrosine-based polymers, poly(methyl vinyl ether), poly(maleic anhydride), poly(glyconates), polyphosphazines, poly(esteramides), polyketals, poly(orthocarbonates), poly(maleic acid), poly(alkylene oxalates), poly(alkylene succinates),
20 poly(pyrrole), poly(aniline), poly(thiophene), polystyrene, non-biodegradable polyurethanes, polyureas, poly(ethylene vinyl acetate), polypropylene, polymethacrylate, polyethylene, poly(ethylene oxide), and co-polymers, adducts, and mixtures thereof.

70. The osteoimplant of claim 59, wherein the silane coupling agent attached to the bone
25 particles is chemically modified.

71. The osteoimplant of claim 70, wherein a moiety selected from a biomolecule, a small molecule, a bioactive agent, a non-biologically active material, and any combination of the above is attached to the silane coupling agent.

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72. The osteoimplant of claim 71, wherein the moiety is linked to the polymer by a member of covalent and non-covalent interactions.

73. The osteoimplant of claim 59, wherein a surface of at least a portion of the bone particles has been chemically modified.

74. The osteoimplant of claim 73, wherein the surface of at least a portion of the bone particles is treated with dilute phosphoric acid.

75. The osteoimplant of claim 59, wherein a composition of at least a portion of the bone particles is modified.

76. The osteoimplant of claim 75, wherein at least a portion of the bone particles are dried, lyophilized, defatted, treatment with a detergent, treatment with a solvent, treatment with a surfactant, or treated to remove or inactivate pathogens.

77. The osteoimplant of claim 59, further comprising a cross-linking agent.

78. The osteoimplant of claim 77, wherein the cross-linking agent is selected from aldehydes, polyepoxy compounds, polyvalent metallic oxides, organic tannins, N-hydroxysuccinimides, N-hydroxysulfosuccinimides, phenolic oxides, hydrazides, carbodiimides, isocyanates, isothiocyanates, sugars and enzymes.

79. The osteoimplant of claim 59, wherein a surface of the composite has been modified.

80. The osteoimplant of claim 79, wherein the modification of a surface of the composite is a member of oxidation of at least a portion of the surface, etching of at least a portion of the surface, retention of a biomolecule on the surface, retention of a small molecule on the surface, retention of a bioactive agent on the surface, and any combination of the above.

81. The osteoimplant of claim 59, further comprising one or more of a wetting agent, biocompatible binder, filler, fiber, plasticizer, biostatic/biocidal agent, surface active agent, biomolecule, small molecule, bioactive agent, and any combination of the above.
- 5 82. The osteoimplant of claim 81, wherein the biologically active agent is selected from antibiotics, chemotherapeutics, bone cell inducers, and bone cell stimulators.
83. The osteoimplant of claim 59, further comprising osteoblasts.
- 10 84. A method for modifying a surface of a construct which incorporates large pieces of bone comprising the step of treating the surface with a coupling agent.